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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/782,721 | 02/12/2001 | H. Michael Shepard | 126745200402 | 5394 |

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EXAMINER

CRANE, LAWRENCE E

ART UNIT PAPER NUMBER

1623

DATE MAILED: 08/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|-------------------------------|--------------------------------|--|
| Office Action Summary | Application No. 09/782,721 | Applicant(s) SHEPARD ET AL. | |
| | Examiner L. E. Crane | Art Unit 1623 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06/09/05 (amdt & RCE).
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 56,57,59-67,69,70,73-79 and 86-89 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 56,57,59-67,69,70,73-79 and 86-89 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 May 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Claims **1-55, 58, 68, 71-72 and 80-85** have been cancelled, claims **56-57, 59-62, 86 and 87** have been amended, the disclosure has not been amended, and no new claims have been added as per the amendment filed June 9, 2005. No additional Information Disclosure Statements (IDSs) have been filed as of the date of this Office action.

Examiner notes applicant has given notice of the filing of a related application identified as US Application No. **10/048,033**. Examiner has located the claims, specification, and abstract within a mislabeled e-DAN document. No further action by applicant is necessary.

Claims **56-57, 59-67, 69-70, 73-79 and 86-89** remain in the case.

Note to applicant: When a rejection refers to a claim **X** at line **y**, the line number “y” is determined from the claim as previously submitted by applicant in the most recent response including ~~lines deleted by line through~~.

Suggestion to applicant: Claims directed to compounds with pharmaceutical potential may be accompanied by one or more
-- pharmaceutical composition claims --.

Claims **62 and 64-67** are objected to because of the following informalities:

In claim **62** at lines 15, 16, 25, 27 and 38, all members of the Markush groups are not properly separated by punctuation. See also claims **64, 65, 66 and 67** wherein the same error also occurs. Consistent punctuational separation is respectfully requested.

In claim **62** at line 26, the N-acyl functionality presently is terminated by a “CH₂” group which leaves open a valence (valence error or typographical error). Did applicant intend the acyl group to be acetyl (CH₃-(C=O)-) ?

In claim **62** at line 43, the term “naturally-occurring” includes a misspelling of the included term -- occurring -- .

In claim **62** at line 33, the term “M is zero” appears to include a typographical error. Did applicant intend the term to read
-- m is zero -- ?

Appropriate correction is required.

Claims **56-57, 59-61, 62-67, 69, 73-79 and 86-89** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one of ordinary skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention; the scope is excessive in view of the disclosed exemplifications.

The compounds encompassed by claim **62** are directed to a vast number of chemical species which have not been described in the instant disclosure in a manner permitting the ordinary practitioner to have the guidance necessary to make, and also how to use, a very large proportion of said species, in part because of the overly broad definitions of substituents. Examiner finds only a limited number of phosphoramidate compounds provided in the "Examples" section and none of these compounds discloses a structure which provides for "derivatives" or "analogues"(line 9 of claim **62**) of the compounds provided for by the noted claim. And in addition, there is insufficient showing in the disclosure and accompanying declaration to support the limitation in the last lines of claim **62** that all "stereoisomeric," "enantiomeric" and "anomeric" forms have been synthesized, or that any reasonably predictive proportion of same have been tested to determine that the claimed pharmaceutical activity occurs in some subset thereof. And lastly, method claims **56, 57 and 86-88**, directed to the treatment of all diseases encompassed by the generic terms "cancer," "autoimmune disorder," and "inflammatory condition" by a compound of claim **62**, is not adequately supported by the test results disclosed by the instant specification as supplemented by the declaration of Dr. Cathers.

The above criticisms are each an indication of excessive claim scope and may be overcome by either narrowing the scope of the claims or by providing additional test data, or a combination thereof.

Applicant's arguments with respect to claims **56-57, 59-61, 62-67, 69, 73-79 and 86-89** have been considered but are deemed to be moot in view of the new grounds of rejection.

Claims **56-59, 61-63, 65, 72, 81-84 and 86-87** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims **56 and 57** at the last two lines, the term “or a metabolite thereof formed after administration to a subject” is indefinite because the particular structure of the active ingredient is not defined thereby rendering the claim incomplete. Alternatively, the term is superfluous because the encompassed subject matter is inherently included within the scope of all method of treatment claims wherein the active ingredient is defined by claim **62**. Deletion is respectfully requested.

In claim **56** at lines 1-2, the term, “pathology characterized by hyperproliferative neoplastic cells,” is indefinite for failure to specify the particular disease or disease vector being referred to; i.e. are the diseases “cancers,” and if so which cancer or cancers? See also claims **57, 86 and 87**. The term “pathological hyperproliferative cell” is no better because it also fails to define the particular disease(s) to be treated.

Applicant’s arguments with respect to claims **56, 57, 86 and 87** have been considered but are deemed to be moot in view of the new grounds of rejection.

In claim **61** the definition of variable R^4 includes subject matter not included within the scope of the equivalent definition found in claim **62**, thereby rendering the the instant claim lacking in proper antecedent basis. In addition, the terms limited by the term “ C_2 to C_4 ” are rendered superfluous thereby because the terms “-O-aryl,” “-O-heteroaryl,” “-S-aryl,” and “-S-heteroaryl” must necessarily include more than 4 carbon atoms and, in the case of “heteroaryl,” said terms are also incomplete because the heteroatom(s) and their location(s) in the rings have not been defined.

Applicant’s arguments with respect to claim **61** have been considered but are deemed to be moot in view of the new grounds of rejection.

In claim **62** at line 9, the term “aromatic C_4X group, wherein X is the heteroatom” is incomplete because the identity of the “heteroatom” has not been defined. Said term is also confusing because of the inconsistency between the terms “aromatic” and “heteroatom,” because the former term is usually understood by the ordinary practitioner to be limited to non-heteroaromatics including phenyl.

Applicant’s arguments with respect to claim **62** have been considered but are deemed to be moot in view of the new grounds of rejection.

In claim **62** at line 11, the term “and” is incorrect because it implies an obvious valence error. Replacement of the noted term with the term -- or -- would overcome the instant rejection.

Applicant’s arguments with respect to claim **62** have been considered but are deemed to be moot in view of the new grounds of rejection.

In claim **62** at lines 43-44, the term “derivative of a naturally-occurring [sic] amino acid” is indefinite due to a lack of defined metes and bounds.

In claim **76** the amino acid “acyl” substituent is either incomplete (open valence at the “CH₂” group suggests an unknown group should be appended thereon) or suffers from a typographical error (“CH₂” should have been -- CH₃ --). See also claim **62** at line 26. Appropriate correction is respectfully requested.

Applicant’s arguments with respect to claims **62 and 76** have been considered but are deemed to be moot in view of the new grounds of rejection.

In claim **86** at lines 5-7, the entire step “(b)” is completely superfluous because once a compound has been administered to a host, there is no control over what happens as a consequence of contact between the active ingredient and the tissues and enzymes of the host. Therefore, deletion of the noted lines in their entirety is respectfully requested. See also claim **87** at lines 7-8 for the same error. Deletion of the noted portions of claims **86 and 87** would render said claims substantial duplicates of claims **56 and 57**.

Applicant’s arguments with respect to claim **86 and 87** have been considered but are deemed to be moot in view of the new grounds of rejection.

The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F. 2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir 1985); and *In re Goodman*, 29 USPQ 2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. §1.78(d).

Effective January 1, 1994, a registered attorney or agent or record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. §3.73(b).

Claims **56-57, 60-61 and 86-89** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim **1-12** of U. S. Patent No. **6,495,553**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treatment and the alleged active ingredients are directed to substantially overlapping subject matter.

Applicant's arguments filed June 9, 2005 have been fully considered but they are not persuasive.

Applicant has acknowledged but has deferred response to this grounds of rejection.

Claims **62-67, 69-70 and 73-79** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **36-39** of U. S. Patent No. **6,339,151**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treatment and the alleged active ingredients are directed to substantially overlapping subject matter.

Applicant's arguments filed June 9, 2005 have been fully considered but they are not persuasive.

Applicant has acknowledged but has deferred response to this grounds of rejection.

Claims **56-57, 59-67, 69-70, 73-79 and 86-89** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1-7** of U. S. Patent No. **6,245,750**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treatment and the alleged active ingredients are directed to substantially overlapping subject matter.

Applicant's arguments filed June 9, 2005 have been fully considered but they are not persuasive.

Applicant has acknowledged but has deferred response to this grounds of rejection.

Claims **56-57, 59-67, 69-70, 73-79 and 86-89** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1-30** or **copending claims** of co-pending Application No. **10/119,927**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds and the methods of treatment are overlapping with the instant claimed subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments filed June 9, 2005 have been fully considered but they are not persuasive.

Applicant has acknowledged but has deferred response to this grounds of rejection.

Claims **56-57, 59-61 and 86-89** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1-22** or **copending claims** of co-pending Application No. **10/051,320** (for the PG PUBS version, see PTO-892 ref. **P3**). Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds and the methods of treatment are overlapping with the instant claimed subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments filed June 9, 2005 have been fully considered but they are not persuasive.

Applicant has acknowledged but has deferred response to this grounds of rejection.

Claims **62-67, 69-70 and 73-79** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1 and 53-83** or

copending claims of co-pending Application No. **10/681,418**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treatment and the alleged active ingredients are directed to substantially overlapping subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments filed June 9, 2005 have been fully considered but they are not persuasive.

Applicant has acknowledged but has deferred response to this grounds of rejection.

Claims **56-57, 59-67, 69-70, 73-79 and 86-89** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1-10** of U. S. Patent No. **6,683,061** (PTO-892 ref. **AB**). Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds and the methods of treatment are overlapping with the instant claimed subject matter.

Applicant's arguments filed June 9, 2005 have been fully considered but they are not persuasive.

Applicant has acknowledged but has deferred response to this grounds of rejection.

Claims **56-57, 59-67, 69-70, 73-79 and 86-89** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1-25** of co-pending US Application No. **10/048,033**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds and the methods of treatment are overlapping with the instant claimed subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments filed June 9, 2005 have been fully considered but they are not persuasive.

Applicant has acknowledged but has deferred response to this grounds of rejection.

Claims **56-57, 59-67, 69-70, 73-79 and 86-89** of this application conflict with claims **1-30** or **copending claims** of co-pending US Application No. **10/119,927** claims **1-22** or **copending claims** of co-pending US Application No. **10/051,320**, claims **1 and 53-83** or **copending claims** of co-pending US Application No. **10/681,418**, and of claims **1-25** of co-pending US Application **10/048,033**. 37 C.F.R. §1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP §822.

Papers related to this application may be submitted to Group 1600 via facsimile transmission(FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX directly to Examiner's computer is 571-273-0651. The telephone number for submission of an official FAX to the USPTO is **(703) 872-9306**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

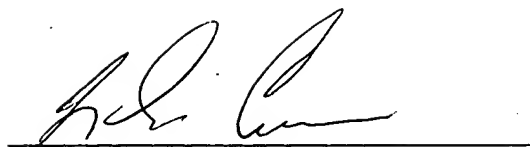
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson, can be reached at **571-272-0661**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

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LECrane:lec
07/28/2005

A handwritten signature in black ink, appearing to read "L. E. Crane", is written over a horizontal line.

L. E. Crane, Ph.D., Esq.
Primary Patent Examiner
Technology Center 1600